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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,296	09/13/2000	Patricia Anne Nuttall	2369-1-002	3816

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,296	NUTTALL ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10,18,20-32,34,42,44,52 and 53* is/are pending in the application.

4a) Of the above claim(s) *2,3,5 and 7* is/are withdrawn from consideration.

5)☒ Claim(s) *1,4,6,10,18,21-24 and 29* is/are allowed.

6)☒ Claim(s) *20,25-28,30-32,34,42,44,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-7,10,18,20-32,34,42,44,52 and 53* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 13 December 2004 has been entered in full. Claims 1, 4, 6, 10, 18, 20-30, 34, 42, and 44 are amended. Claims 8-9, 11-17, 19, 33, 35-41, 43, and 45-51 are cancelled. Claims 52-53 are added.

This application contains claims 2-3, 5, 7 are drawn to an invention nonelected without traverse in the communication of 04 April 2003, 02 September 2003, and 19 November 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4, 6, 10, 18, 20-32, 34, 42, 44, and 52-53 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 3 of the previous Office Action (10 June 2004) are *withdrawn* in view of the submitted abstract and amended specification (13 December 2004).

2. The objections to claims 1, 4, 6, 10, 18-21, 25-30, 32-34, and 39-44 at pg 4 of the previous Office Action (10 June 2004) is *withdrawn in part* in view of the amended and cancelled claims (13 December 2004). Please see section on Claim Objections, below.

3. The rejections of claims 1, 4, 6, 10, 18-34, and 39-44 under 35 U.S.C. § 101 (product of nature; improper process claim) as set forth at pg 4 and 17 of the previous Office Action (19 June 2004) are *withdrawn* in view of the amended and cancelled claims (13 December 2004).

4. The rejection of claims 1, 4, 6, 10, 18-24, and 29 under 35 U.S.C. § 112, first paragraph (scope of enablement) as set forth at pg 5-8 of the previous Office Action (10 June 2004) is *withdrawn* in view of the cancelled claims, amended claims, and Applicant's persuasive arguments (13 December 2004).

5. The rejection of claims 25-28, 39-34, and 39-44 under 35 U.S.C. § 112, first paragraph (total lack of enablement) as set forth at pg 8-12 of the previous Office Action (19 June 2004) is *withdrawn in part* in view of the cancelled claims (13 December 2004) and consideration of post-filing date reference Couillin et al. (J Immunol 173: 3281-3286, 2004). Please see 35 U.S.C. § 112, first paragraph (scope of enablement), below.

6. The rejection of claims 1, 4, 6, 10, 18-34, and 39-44 under 35 U.S.C. § 112, first paragraph (written description) as set forth at pg 12-14 of the previous Office Action (10 June 2004) is *withdrawn* in view of the cancelled claims, amended claims, and Applicant's persuasive arguments (13 December 2004).

7. The rejections to claims 1, 4, 6, 10, 18-34, and 39-44 under 35 U.S.C. § 112, second paragraph, as set forth at pg 14-17 of the previous Office Action (10 June 2004) are *withdrawn* in view of the amended and cancelled claims (13 December 2004). Please see 35 U.S.C. § 112, second paragraph, below.

8. The rejection of claims 1, 4, 19, 21-22, 24, 29-30, 33-34, 39, and 41-44 under obviousness-type double patenting as set forth at pg 17-18 of the previous Office Action (10 June 2004) is *withdrawn* in view of the cancelled claims and submission of a terminal disclaimer (13 December 2004).

Sequence Compliance

9. The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (13 December 2004) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (10 June 2004) are withdrawn.

Claim Objections

10. Claim 32 is objected to because of the following informalities:

10a. Claims 32 recites a non-elected species. The basis for this objection was set forth at pg 4 of the previous Office Action. Applicant asserts that claim 32 has been amended to address this issue, thereby rendering moot the objection to this claim. However, claim 32 has not been amended to recite the elected species of cysteinyl leukotriene.

Claim Rejections - 35 USC § 112, first paragraph

11. Claims 20, 25-28, 30-32, 34, 42, 44, and 52-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preventing or treating allergic asthma comprising administering an isolated histamine or serotonin binding protein of claim 1 to a human or animal wherein said protein prevents or treats allergic asthma, does not reasonably provide enablement for (a) a method of treating or preventing a disease condition related to a vasoactive amine, (b) a method for treating or preventing inflammation or allergic reaction, and (c) a method for treating or preventing a disease condition related to serotonin activity comprising administering an isolated histamine or serotonin binding protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection was set forth for claims 25-28, 30-34, and 39-44 at pg 8-12 of the previous Office Action (10 June 2004). It is noted that Couillin et al. (J Immunol 173: 3281-

3286, 2004) teaches that FS-HBP2 prevents allergic asthma in mice (pg 3282, col 2 through pg 3284). FS-HBP2 (also disclosed in the instant specification) and the D.RET6 protein of SEQ ID NO: 4 are similar in structure and histamine binding sites/residues (see Figure 22 of the instant specification for alignment; pg 81 of Sangamnatdej et al., already made of record).

The claims are directed to a histamine or serotonin binding protein associated with one or more carbohydrate moieties or with one or more peptides or polypeptides. The claims recite that the protein has a toxin or bioactive molecule or reporter molecule attached thereto. The claims recite that the protein additionally comprises a cysteinyl leukotriene. The claims recite a method for treating or preventing a disease condition related to a vasoactive amine by administering the histamine or serotonin binding protein. The claims recite a method for treating or preventing inflammation or allergic reaction in humans or animals by administering an isolated histamine or serotonin binding protein. Additionally, the claims are drawn to a method for treating or preventing a disease condition related to serotonin activity by administering an isolated histamine or serotonin binding protein.

Applicant's arguments (13 December 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the claims are directed to a histamine or serotonin binding protein comprising SEQ ID NO: 4 and having the recited properties. Applicant submits that the rationale behind fusion of a histamine or serotonin binding protein with a further moiety is not to create a new activity brought about by the association of the two moieties. Rather, the rationale is to bring together two moieties in a fusion protein, such that each moiety contributes the functional activity/activities exhibited when in isolation and the fusion protein exhibits a

combination of these desired activities. Applicant states that techniques for the preparation of fusion proteins are well documented in the art and the preparation of fusion proteins is a matter of routine practice.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, Applicant is arguing limitations that are not present in the instant claims. The claims must independently define the invention for which patent protection is sought. The specification does not provide any guidance as to how use the fusion histamine or serotonin binding proteins with multiple activities. Undue experimentation would be required of one skilled in the art to fuse a histamine or serotonin binding protein with any carbohydrate, protein, toxin, or bioactive molecule and screen them for activity. The broad brush discussion of making and screening for fusion proteins does not constitute adequate guidance to practice the claimed invention, but rather constitutes an invitation to experiment empirically to obtain the fusion proteins required by the claims.

Additionally, it is noted that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37; *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

(ii) Applicant contends that the Examiner appears to be suggesting that *in vivo* evidence must be disclosed to support a claim relating to the therapeutic use of a compound. Applicant submits that provided there is no technical information missing from the specification for the skilled reader to be able to practice the invention, the specification should be regarded as being enabling. Applicant indicates that possible modes of administration are outlined in the specification at pg 14, lines 3-10. Applicant asserts that as is evident from the specification, the link between histamine and serotonin release and inflammation is well documented. Applicant argues that the compounds which bind to histamine and serotonin and make it unavailable for binding to histamine and serotonin receptors are expected to be beneficial in the treatment of inflammation. Applicant asserts that corroborative evidence pertaining to the efficacy of two of the related, non-elected compounds to treat inflammation (FS-HBP2 and MS-HBP) is also presented in Exhibits B and C. Applicant adds that the efficacy of using FS-HBP2 and MS-HBP1 for treating two types of allergic reaction, allergic conjunctivitis and allergic rhinitis is clearly demonstrated in results shown in Exhibit B.

Applicant's arguments have been fully considered but are not found to be persuasive. Although Applicant need not actually have reduced the invention to practice prior to filing the application, the lack of a working example is only one factor to be considered, especially in a case involving an unpredictable art (MPEP § 2164.02). The specification at pg 12-16 outlines prophetic examples for administering a histamine or serotonin binding compound for the treatment of various conditions or disorders. However, this is not adequate guidance, but is merely an invitation for the skilled artisan to use the current invention as a starting point for further experimentation. The claimed method may not necessarily treat or prevent inflammation,

allergic reaction, a disease condition related to a vasoactive amine, and a disease condition related to serotonin activity. The skilled artisan must resort to trial and error experimentation to identify individuals with these conditions as well as the optimal dosage, duration, and mode of administration of the claimed histamine or serotonin binding protein. Such trial and error is considered undue. Additionally, the various diseases and disorders disclosed in the claims (inflammation, allergic reaction, a disease condition related to a vasoactive amine, and a disease condition related to serotonin activity) have different pathophysiologies. For example, systemic lupus erythematosus is a chronic rheumatic disease with many clinical presentations, which may lead to inflammation and damage to various body organs (Ioannou et al., Postgrad Med J 78: 599-606, 2002; pg 599, abstract, col 1). The mechanisms causing the disease are still unknown (Ioannou et al., pg 599, ¶ 3). Carcinoid tumors are thought to arise from neuroendocrine cells and are found to contain numerous membrane-bound neurosecretory granules. The granules are composed of a variety of hormones and biogenic amines (Kulke et al. New Engl J Med 340:858-868, 1999). The carcinoid tumors excrete serotonin, corticotrophin, histamine, dopamine, substance P, neurotensin, prostaglandins, and kallikrein, all of which cause carcinoid syndrome (episodic flushing, wheezing, diarrhea, right-sided valvular heart disease) (pg 585 of Kulke et al., 3rd full paragraph). Therefore, undue experimentation would be required of the skilled artisan to administer a histamine or serotonin binding protein to individuals with all possible types of inflammation, allergic reaction, disease conditions related to a vasoactive amine, and disease conditions related to serotonin activity (which have different pathophysiologies) and treat the disorder or disease. Undue experimentation would also be required of the skilled artisan to diagnose a condition using a histamine or serotonin binding protein of the instant claims since

the specification does not teach any diseases or conditions that are associated with an overexpressed or underexpressed histamine or serotonin binding protein.

Although Applicant indicates that evidence pertaining to the efficacy of two of the related, non-elected compounds (FS-HBP2 and MS-HBP) to treat inflammation, allergic reaction, allergic conjunctivitis and allergic rhinitis is presented in Exhibits B and C, Applicant's argument is not persuasive because the evidence in the Figures and text of Exhibits B and C must be submitted in the form of a declaration under 37 C.F.R. 1.132. An unpublished manuscript and/or graphs are not proper evidence, since they have not been peer-reviewed and their contents have not been attested to under 37 CFR 1.132. Without submission under 37 C.F.R. 1.132 , it is unclear where the data in the text and graphs originate from. However, if submitted under 37 C.F.R. 1.132, the results in the manuscript/graphs would still not be persuasive. Specifically, the examples and evidence in Exhibits B and C are not commensurate in scope with the instant claims.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate and screen histamine/serotonin binding compounds fused with carbohydrate moieties, proteins, toxins, or bioactive molecules for activity and to determine the quantity of histamine or serotonin binding compound to be administered, the most effective administration route, and the duration of the treatment for the treatment or prevention of all possible types of inflammation, allergic reaction, disease conditions related to a vasoactive amine, and disease conditions related to serotonin activity; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention; and the

unpredictability of preventing all possible types of inflammation, allergic reaction, disease conditions related to a vasoactive amine, and disease conditions related to serotonin activity, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112

12. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. The term "bioactive molecule" in claim 20 is a relative term which renders the claim indefinite. The term "bioactive molecule" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It cannot be determined what compounds are encompassed by the term "bioactive molecule" or what specific activity they possess.

Conclusion

Claims 1, 4, 6, 10, 18, 21-24, 29 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
28 April 2005

ELIZABETH KEMMERER
PRIMARY EXAMINER